# Amyloids & exosomes:

## Unravelling their functional relationship

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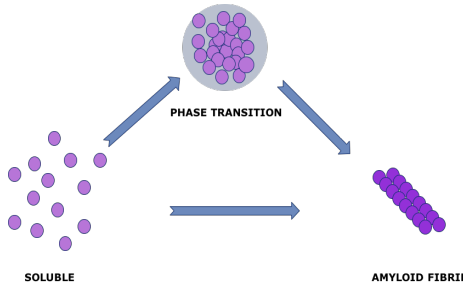
## 1. Introduction

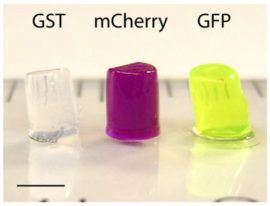
Exosomes have been reported as a not well characterized amyloid spreading pathway with an increasing impact on the onset of neurodegenerative diseases. With the recent rising of functional amyloids, an integrative understanding of amyloids as a biological entities and not only as illness sources is in need. Thus, the amyloid enrichment in exosomes might be the noticeable part of a functional relationship. The exosome delivery of information in form of proteins and RNA would be more efficient by exploiting this kind of macromolecular assemblies.

In this work, the current breakthroughs in the field are explored in order to propose a new interpretation of this apparently harmful interaction.

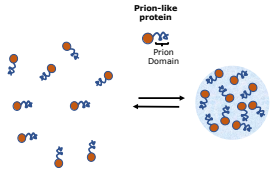
## 2. Amyloids and other structures




**Different stages in amyloid folding. The phase transition is a metastable state between the soluble protein and the amyloid fibril.**

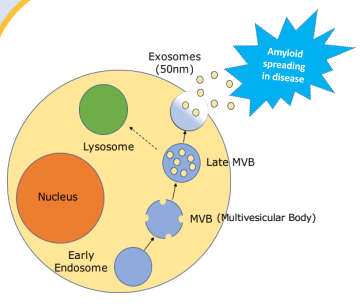


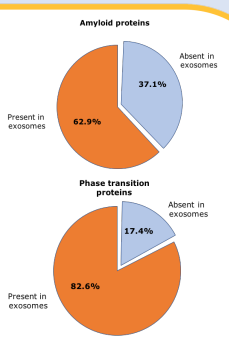

**In vitro polymerization of prion-like proteins. (image extracted from Kato et al. 2012)**



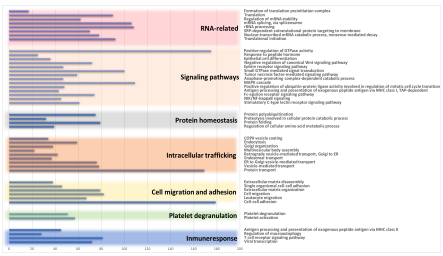

**Prion-like proteins undergo phase transition to form membrane-less compartments in vivo.**

## 3. Exosomes and amyloid enrichment

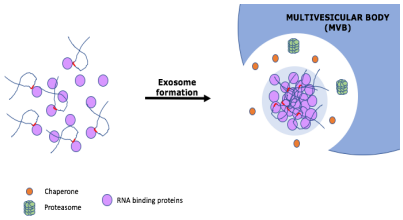



**Gene ontology enrichment by Biological process in exosome protein cargo**



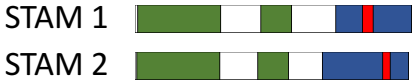

## 4. Are phase transition proteins involved in RNA packaging?




**The formation of membrane-less compartments would allow the customization of the exosome cargo. The quick switch between states leads to a faster regulation than at transcriptional level.**

## 5. Identification of novel prion-like domains

**The paralog proteins STAM1 and STAM2, involved in signalling pathways, might be regulated using prion-like domains. The amyloid assembly might be a rational way of protein delivery.**




**Putative prion domains (PPrD) in blue, the amyloid core in red and their pFam domains in green.**

## 6. Applications

The amyloid structure is a very useful and versatile tool, and their functional implications in the cell are just beginning to be studied. The hypothesis here exposed exemplify the wide range of possibilities of these macromolecular structures. Exosomes are now intensively studied as a target-specific carrier due to their high stability, minimal immunogenicity and their ability to cross the blood brain barrier. Promising therapeutic approaches could profit from the natural relation of these two entities:

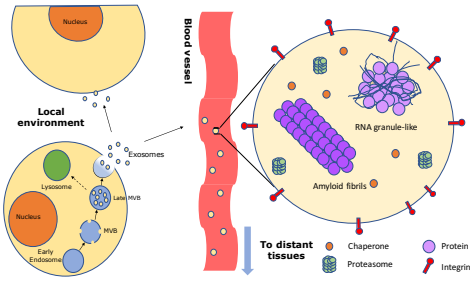
- The understanding of RNA granules in exosomes could be used to optimize the RNA loading, which is a limited factor in siRNA therapies using exosomes.
- The deliver of proteins in form of inert amyloids might avoid toxicity both in sending and receptor cells and optimize the space and organization inside the exosome.

During the development of this work, an exosome database was assembled and enriched with the generated information. The aim of this web page is to make available an easy-to-use database containing the exosome protein cargo, that it also include the prion-predictions. All the data is available in form of a browser in the EXOAMYL web-page.

**EXOAMYL**

www.exoamyl.weebly.com


## 7. Integrative model

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